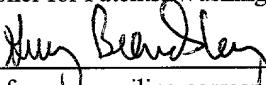


PATENT
ATTORNEY DOCKET NO. 50025/003002

Certificate of Mailing	
Date of Deposit <u>April 19, 2001</u>	Label Number: <u>EL509219083US</u>
I hereby certify under 37 C.F.R. § 1.10 that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" with sufficient postage on the date indicated above and is addressed to BOX PATENT APPLICATION, Assistant Commissioner for Patents, Washington, D.C. 20231.	
<u>Guy Beardsley</u> Printed name of person mailing correspondence	 Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Victor J. Dzau *et al.* Art Unit: Not Yet Assigned
Serial No.: Not Yet Assigned Examiner: Not Yet Assigned
Filed: April 18, 2001
Title: Therapeutic Use of Cis-Element Decoys *In Vivo*

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT AND REMARKS

Applicants submit the following Amendment and Remarks for consideration prior to examination of the above-captioned patent application.

AMENDMENT

Kindly amend the application as follows.

In the Claims:

Cancel claims 1-12, without prejudice, and add the following new claims 13-16.

13. (New) A method for inhibiting proliferative lesion formation in a blood vessel, said method comprising introducing into vascular smooth muscle cells of said blood vessel dsDNA that comprises a sequence that is specific for binding to transcription factor E2F, in an amount sufficient to inhibit proliferative lesion formation in said blood vessel.

14. (New) The method of claim 13, wherein said blood vessel is within a mammal.

15. (New) The method of claim 14, wherein said mammal is a human.

16. (New) The method of claim 13, wherein said dsDNA is introduced into said vascular smooth muscle cells of said blood vessel *ex vivo*.

REMARKS

The amendment set forth above adds to the application independent claim 13, as well as several claims that depend from claim 13. New claim 13 is drawn to a method of inhibiting proliferative lesion formation in a blood vessel, in which dsDNA that includes a sequence that binds to transcription factor E2F (*i.e.*, an E2F decoy) is introduced into vascular smooth muscle cells of the blood vessel. Claim 13 is similar to claim 8 of the parent application, U.S. Serial No. 08/524,206, except that claim 13 is narrower in that it specifies the use of a decoy to a particular transcription factor, E2F.

Claim 8 was not rejected over the prior art in the parent application. Moreover, the operability of the subject matter of claim 8, employing an E2F decoy, as is specified in claim 13, is shown in the enclosed paper by Mann *et al.*, The Lancet 354:1493-1498, 1999. Briefly, this paper describes human clinical studies in which E2F decoys were introduced into human infrainguinal vein grafts. As is discussed in the paper, fewer proliferative lesions, such as graft occlusions, revisions, and critical stenoses, were observed in patients having E2F decoy-treated grafts as compared to untreated controls. Consistent with this observation, the levels of proliferating-cell nuclear antigen and *c-myc* mRNA, which each is an indicator of cellular proliferation and, in the vasculature, can lead to proliferative lesion formation, were decreased in E2F decoy-treated grafts, as compared to untreated controls. These human clinical data show that E2F decoys are effective in inhibiting proliferative lesion formation in human blood vessels, as is

specified in new claims 13-16.

CONCLUSION

Although no charges are believed to be due, if there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: April 19, 2001

Susan M. Michaud
Susan M. Michaud, Ph.D.
Reg. No. 42,885

Clark & Elbing LLP
176 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045
50025.003002 preliminary amendment.wpd



21559
PATENT TRADEMARK OFFICE